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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 0817/000006	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP99/05467	International filing date (*day/month/year*) 30 July 1999 (30.07.99)	Priority date (*day/month/year*) 05 August 1998 (05.08.98)
International Patent Classification (IPC) or national classification and IPC C12N 15/53, 15/54, 15/82, 9/10, 9/04, C12Q 1/02, A01H 5/00		
Applicant SUNGENE GMBH & CO.KGAA		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
24 February 2000 (24.02.00)	18 October 2000 (18.10.2000)
Name and mailing address of the IPEA/EP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/EP99/05467

I. Basis of the report

1. This report has been drawn on the basis of (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

☐ the international application as originally filed.

☒ the description, pages 1-48, as originally filed,
pages _____, filed with the demand,
pages _____, filed with the letter of _____,
pages _____, filed with the letter of _____.

☒ the claims, Nos. _____, as originally filed,
Nos. _____, as amended under Article 19,
Nos. _____, filed with the demand,
Nos. 1-22, filed with the letter of 25 September 2000 (25.09.2000),
Nos. _____, filed with the letter of _____.

☒ the drawings, sheets/fig 1/11-11/11, as originally filed,
sheets/fig _____, filed with the demand,
sheets/fig _____, filed with the letter of _____,
sheets/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

4. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/EP 99/05467

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-17, 19-22	YES
	Claims	18	NO
Inventive step (IS)	Claims		YES
	Claims	1-22	NO
Industrial applicability (IA)	Claims	1-22	YES
	Claims		NO

2. Citations and explanations

1. This report makes reference to the following documents:

D1: LANGE B.M. ET AL.: P.N.A.S. USA, (1998 MAR 3) 95 (5) 2100-4.

D2: MANDEL A. ET AL.: PLANT JOURNAL, Vol. 9, No. 5, 1996, pp. 649-658

D3: EP-A-0 723 017

D4: WO-A-97/27285

D5: WO-A-98/06862

D6: LOIS L.M. ET AL.: P.N.A.S. USA (1998 MAR 3) 95 (5) 2105-10

D7: SPRENGER G.A. ET AL.: P.N.A.S. USA (1997 NOV 25) 94 (24) 12857-62

D8: KELLER ET AL.: EUROP. J. BIOCHEM., Vol. 251, No. 1/02, pp. 413-417

D9: WO-A-99/11757, 11 March 1999

D10: DE-A-197 52 700, 2 June 1999

2. This report is based on the assumption that all of the claims enjoy the priority of the priority document filing date. Should it later become clear that this is not the case, documents D9 and D10, cited in the international search report, would

become relevant.

3. Novelty

Claim 18 lacks novelty over *Arabidopsis* plants, which naturally contain the cited expression cassette (cf. D2).
The expression "transformed" indicates only that the plant is a product of a transformation process, without implying a clear, differentiating feature that would establish novelty.

4. Inventive step

The present application does not meet the criterion stipulated by PCT Article 33(3), because the subject matter of Claims 1-17 and 19-22 does not involve an inventive step.

4.1 Document D1 discloses the cloning of the 1-deoxy-D-xylose-5-phosphate synthase (DOXS), which catalyzes the first reaction of the mevalonate-independent synthesis pathway of isopentenyl pyrophosphate (IPP), from the plant *Mentha x piperita*. Said document also proposes the transgenetic manipulation, made possible thereby, of isoprenoid biosynthesis in plants, as well as its use in the design of herbicides (cf. page 2104, last paragraph).

The subject matter of Claims 1, 2 and 9 differs from the above only in that it specifies which isoprenoids are formed from the transgenetic plants in increased numbers, namely tocopherol, vitamin K, chlorophyll and/or carotinoids. However, a person

skilled in the art would know, based on general knowledge, that these isoprenoids are formed in plants, from IPP. Consequently, Claims 1, 2 and 9 lack an inventive step.

4.2 Furthermore, it is pointed out that Claims 1, 2 and 9 also fail to be inventive in the light of D4. D4 discloses the use of a DNA sequence that codes for the enzyme HPPD, for producing plants containing increased amounts of vitamin E and carotinoid. HPPD is also suggested as a starting point for herbicides.
The subject matter of Claims 1, 2 and 9 differ herefrom in that the enzyme DOXS is used in place of HPPD. However, in light of D1, it would have been obvious to a person skilled in the art that the DOXS gene could also be used as an alternative to HPPD. Although it is not possible to predict with 100% accuracy whether the introduction of a specific gene will have the desired effect, in the present case and in light of the prior art, a person skilled in the art could, however, reasonably expect that the use of the DOXS gene would in fact lead to an increase in the amount of tocopherol, vitamin K, chlorophyll and/or carotinoid contained in plants.

4.3 Claims 3-8, 10-12 and 14-16 pertain to uses or methods in which the DOXS gene is combined with the gene that codes for the p-hydroxyphenol pyruvic acid dioxygenase (HPPD) and/or with the gene that codes for geranylgeranyl pyrophosphate oxidoreductase (GGPPOR). However, this cannot be regarded as involving an inventive step, since the function and effect of these enzymes were known from the prior art (cf. D4 or D8).

4.4 The method according to Claim 13 uses the *Arabidopsis* or *E-coli* DOXS gene. However, it would be obvious to a person skilled in the art to use the *Arabidopsis* or *E-coli* DOXS genes known from D2, D6 and D7 in the same way as the corresponding *Mentha* gene proposed in D1. Consequently, Claims 17-22 (insofar as they are novel) lack an inventive step.

4.5 In addition, Claims 20 and 21 fail to be inventive because it would also be obvious in light of D3 to use the transketolase known from D1 to identify inhibitors.

4.6 The applicant has argued that the claimed subject matter involves an inventive step because there are many biosynthesis steps to go through between the overexpressed gene and the desired end product, and that based on the many metabolic pathways it is neither predictable nor possible to expect with a reasonable degree of certainty that the overexpression would lead to an increase. The applicants state that it is known from many works (which were not described in detail) that, owing to various regulating mechanisms, even the overexpression of very close biosynthesis genes does not automatically cause an increase in a desired end product.

Above all, it must be said that the application itself shows only that the overexpression of DOXS and, as the case may be, of HPPD and/or GGPPOP, in rapeseed leads to an increase in the α-tocopherol concentration. The result as regards the chlorophyll and carotinoid content could also be a decrease, as

is clear from Table 2 on page 33 of the description.

If one were to follow the (unsubstantiated) argumentation of the application, it would have to be assumed that the result is an increase only in the α-tocopherol concentration and not in that of vitamin K, chlorophyll or carotinoid. However, fundamentally, an inventive step can only be recognized based on a surprising effect verified by the applicant if it is convincingly argued that this effect actually does exist throughout the entire scope of claimed subject matter.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

5. The application does not meet the requirements of PCT Article 6 because the claims are not clear.

5.1 The expression "hybridizing DNA sequence" used in Claims 2, 4, 6, 8-12 and 22 is, without an indication of the exact hybridization conditions, vague and unclear and leaves the reader unsure as to the meaning of the technical feature in question. As a result, the definition of the subject matter is not clear (PCT Article 6).

Claims 9-12 and 22 are particularly unclear because these claims do not even define the function of the coded protein. These claims also fail to indicate the essential features of the invention and do not meet the requirement of PCT Article 6 in conjunction with PCT Rule 6.3(b) according to which each independent claim must include all the technical features that are necessary for the definition of the invention.

5.2 Although Claims 1 and 2, 3 and 4, 5 and 6, and 7 and 8 were drafted as separate, independent claims, they appear to in fact pertain to one and the same subject, and clearly they differ from each other only by different definitions of the subject for which protection is sought. Thus the claims are not concise. Further, the claims lack overall clarity since, owing to the numerous independent claims, it is difficult to determine the subject for which protection is sought, such that it is prohibitively

VIII. Certain observations on the international application

difficult for a third party to determine the scope of the subject for which protection is sought. For this reason, Claims 1-8 do not meet the requirements of PCT Article 6.

Furthermore, Claim 2 (4, 6, and 8) contains all of the features of Claim 1 (3, 5, and 7) and is therefore not correctly drafted as a claim dependent on the previous claim (PCT Rule 6.4).